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PATENT SPECIFICATION

NO DRAWINGS

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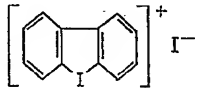
COMPLETE SPECIFICATION

Improvements in or relating to Antibacterial and Antifungal Compositions

We, SMITH KLINE & FRENCH LABORATORIES, of 1500, Spring Garden Street, City of Philadelphia, Zone 1, Commonwealth of Pennsylvania, United States of America, a corporation organized under the laws of the Commonwealth of Pennsylvania, one of the United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to antibacterial and antifungal compositions, to methods of employing such compositions, and to methods and compositions for imparting antifungal and antibacterial properties to surfaces and objects.

This invention is based in part upon the discovery of the surprisingly high germicidal and fungicidal activity of dibenziodolium iodide:



This activity embraces a wide spectrum of micro-organisms including Gram positive and Gram negative bacteria as well as various fungi. Thus for example, dibenziodolium iodide exhibits substantial activity against *Pseudomonas, Escherichia coli, Proteus vulgaris, Micrococcus pyogenes, Diplococcus pneumoniae, Klebsiella pneumonia,* and *Trichophyton mentagrophytes.*

A particularly advantageous aspect of this invention is the extremely low solubility of this compound in water and in most organic solvents. Thus compositions and materials which have been impregnated or coated with dibenziodolium iodide according to this invention are endowed with antibacterial and antifungal properties and these properties are not substantially diminished by contact with most organic solvents, aqueous solutions or body fluids.

Thus according to one aspect of the present invention there is provided an antibacterial and antifungal composition for topical use comprising dibenziodolium iodide and an inert pharmaceutical carrier other than dimethyl formamide.

According to another aspect of the invention, there is provided an impregnating solution having antibacterial and antifungal activity comprising benziodolium iodide and a solvent selected from dimethyl sulfoxide, sulfolanes, acetone or polyethylene glycol.

Dibenziodolium iodide can be employed according to this invention to impart germicidal and fungicidal properties to various absorbent and nonabsorbent surfaces by incorporation in such substances as waxes, polishes, cleaning solutions, disinfectant solutions, paints, detergents and shampoos. It is apparent that the use of such compositions for their usual function will at the same time deposit a residual amount of dibenziodolium iodide in or on the particular substance being treated. Thus waxes, polishes, detergents and paints which contain dibenziodolium iodide are particularly valuable for use in hospitals, nurseries, operating rooms, physician's offices, homes and farms. For example, a coating liquid such as wax or polish when applied to a surface such as the floor of a hospital, aids in combatting the growth or transport of microorganisms, even after the surface has been repeatedly washed.

This invention also embraces the impregnation with dibenziodolium iodide of absorbent material used in articles for personal or surgical use which often serve as the sites for bacterial or fungal growth. Thus dibenzio-

dolium iodide may be employed to impregnate bandages, surgical dressing, sutures, sanitary napkins, plasters, underpads, lavatory tissue, facial tissue, clothing and undergarments.

Solutions of dibenziodolium iodide are preferably employed for impregnation so as to impart a concentration of from 2 mcg./cm.^{2} to 500 mcg./cm^2. It is to be noted that the higher concentration is not the maximum but rather the point at which increased amounts of the compound do not appreciably increase activity. Higher concentrations however such as 1 mg./cm.^{2} are not only operable but often desirable, particularly when employed in a coating of inanimate objects which receive heavy duty such as floors.

For the purpose of impregnation, suitable solvents include dimethyl sulfoxide, sulfolanes, for example 3 - [N - (2 - hydroxyethyl)-N - methylamido] - sulfolane, 3 - amino-sulfolane, and 3-methoxysulfolane, acetone and polyethylene glycol. The particular article is treated with such a solution by immersion or spraying and the solvent then evaporated by application of heat and/or vacuum.

For preparations such as waxes where only temporary dispersion is required, the active ingredient may be temporarily suspended by ultrasonic emulsification or by manual shaking immediately before application.

In addition to the use of the invention in coating or impregnating inanimate objects, dibenziodolium iodide is useful as an antimicrobial agent for topical application for pharmaceutical use in both human and veterinary medicine. For such purposes, a fluid preparation such as powder, ointment, cream, solution, suspension or aerosol is employed. Particularly advantageous pharmaceutical carriers include polyethylene glycol, petrolatum, sulfolanes and Carbowax. The word " Carbowax " is a Trade Mark.

Dibenziodolium iodide is preferably employed in such fluid embodiments of this invention in a concentration of from 5 mcg./ml. to 400 mcg./ml. While higher concentrations may be employed, no appreciable improvement in antimicrobial activity is observed, even at levels as high as 0.2 g./ml. Dibenziodolium iodide is nontoxic and nonirritating at the preferred concentration and possesses a wide margin of safety, exhibiting no irritation or systemic effects, even at high concentrations.

Dibenziodolium iodide is also advantageously incorporated in various solid substances such as plaster casts, deodorant sticks, aftershave sticks, soaps, cosmetics and detergents. In this respect dibenziodolium iodide is incorporated by intimate mixture in the preparation prior to solidification at concentrations of from 5 mcg./ml. to 400 mcg./ml. and the preparation then allowed to solidify in its normal course.

It is to be appreciated that this invention pertains to the deposition of a relatively permanent antibacterial and antifungal agent on any surface other than human skin where microorganism growth is not desired.

The following Examples illustrate the various aspects of the invention.

EXAMPLE 1.

To 46.5 g. of 2,2^1-diaminobiphenyl in 260 ml. of concentrated hydrochloric acid and 250 ml. of water at 5° C is added with stirring a solution of 37 g. of sodium nitrite in 125 ml. of water. The mixture is stirred for 15 minutes and a solution of 130 g. of potassium iodide in 250 ml. of ice and water is then added. After allowing the reaction mixture to stand for three hours at room temperature, an excess of sodium bisulfite solution is added, and the mixture permitted to stand overnight. Upon filtration, the solid collected is sequentially washed with sodium bisulfite, water and cold methanol and then dried to yield dibenziodolium iodide, m.p. 221—222° C, Calc: C 35.50; H 1.99; I 62.52; Found: C 35.57; H 2.16; I 62.21.

EXAMPLE 2.

Well bleached cotton of plain weave having a warp of 44 and a filling of 36 with an average width of 38.5 inches is soaked in a 1% solution of dibenziodolium iodide in dimethyl formamide. The solvent is then removed and the gauze then washed with sterile water and dried.

The finished gauze may also be employed in the preparing of multiple gauze pads.

EXAMPLE 3

Deodorant Stick

Ingredient	Quantity
A.	
*Hystrene T—70 Fatty Acid	5 g.
Sorbo (70% aqueous sorbitol solution)	2 g.
Ethyl Alcohol	85.36 g.

* Hystrene T—70 is a commercially available hydrogenated tallow fatty acid comprising 70% stearic acid and 30% palmitic acid.

B.	
Sodium Hydroxide	0.6 g.
Water	5.0 g.
C.	
Dibenziodolium Iodide	50 mg.

The ingredients (A) are mixed and heated to 65° C and ingredients (B) are mixed and heated to 70° C. The two are combined with agitation and dibenziodolium iodide is then added with stirring. The hot melt is poured into molds and cooled slowly to prevent formation of air pockets. The resultant deodorant sticks are wrapped in foil and packaged in airtight containers. The word "Hystrene" is a Trade Mark.

EXAMPLE 4

Ointment

Ingredient	Quantity
Stearic Acid	20.0 g.
Span 60	10.4 g.
Span 80	2.0 g.
Tween 20	5.6 g.
Distilled Water	138.0 ml.
Dibenziodolium Iodide	5000 mcg.

The fatty materials and emulsifiers are combined with the water and the mixture autoclaved for 20 to 30 minutes at 17 lb./in.^{2} steam pressure. When nearly cool, the dibenziodolium iodide is added and the mixture is agitated thoroughly and worked into a creamy ointment.

The words "Span" and "Tween" are Trade Marks.

EXAMPLE 5

Soap

Ingredient	Quantity
20% Aqueous Coconut Oil Soap Solution	98 g.
Water-soluble Lanolin Derivative (Atlas G—1441)	2 g.
Dibenziodolium Iodide	500 mg.

The water-soluble lanolin derivative is heated to 65° C and the coconut oil soap solution at a temperature of 67° C is added with agitation. Dibenziodolium iodide is next added with agitation and the mixture poured into molds and allowed to cool. The word "Atlas" is a Trade Mark.

EXAMPLE 6

Wax

Ingredient	Quantity
Carnauba Wax	1 lb.
Paraffin Wax	1/4 lb.
Raw Linseed Oil	1/2 pt.
Turpentine	1/2 pt.
Dibenziodolium Iodide	40 g.

The ingredients are heated to 85° C and naphtha is added to make a total volume of 2 gallons. One ounce of ammonium linoleate is added and the mixture stirred until cool. The final wax should be thoroughly shaken before application.

EXAMPLE 7

Polish

Ingredient	Quantity
Crude Montan Wax	50 g.
Solt Ozokerite	20 g.
Paraffin Wax (50—52° C.)	30 g.
Dibenziodolium Iodide	.75 g.

The ingredients are heated and stirred until a smooth emulsion is formed. The mixture is then cooled and packaged.

EXAMPLE 8.

Surgical crinoline is sprinkled with plaster of Paris containing 2% dibenziodolium iodide while being rolled. The crinoline loose plaster bandage is then rolled and employed in the formation of casts or splints.

WHAT WE CLAIM IS:—

1. An antibacterial and antifungal composition for topical use comprising dibenziodolium iodide and an inert pharmaceutical carrier other than dimethyl formamide.

2. A composition as claimed in Claim 1, wherein the carrier is an ointment or wax base.

3. An impregnating solution having antibacterial and antifungal activity comprising dibenziodolium iodide and a solvent selected from dimethyl sulfoxide, sulfolanes, acetone or polyethylene glycol.

4. An antibacterial and antifungal composition substantially as described in any one of the foregoing Examples 2 to 8.

5. An absorbent material having impregnated therein dibenziodolium iodide.

6. A solid substance having incorporated therein dibenziodolium iodide.

7. A method of imparting antibacterial and antifungal properties to an inanimate surface, wherein dibenziodolium iodide is deposited on said surface.

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